

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Attorney Docket No.0512-1334)

First Named Inventor:)
BIBETTE) Confirmation No. 1893
Serial No.: 10/575,449) Before the Examiner:
J.) BLANCHARD, David
Filed: June 13, 2006)
For: Monodispersed solid) Art Unit: 1611
lipid particle compositions)

DECLARATION UNDER RULE 132

To Honorable Commissioner of Patents and Trademarks
Washington, D.C.

Sir :

I, Jérôme BIBETTE, of 40 Rue de Seine 75006 Paris,
FRANCE do solemnly declare:

THAT I have been working with lipid and colloidal
particles for about 20 years and that I now hold the
position of professor at ESPCI in Paris;

THAT, I have read and understood the Office Action
of April 17th, 2009 in connection with the present patent
application as well as the cited prior art;

THAT, the person skilled in the art, willing to
obtain composition fluid, would not have been incited to
add crystallisable lipid components according to Westesen
in the emulsions of Jansen;

THAT, crystallisable lipid components according to Westesen in the emulsions of Jansen would increase the viscosity of the composition;

THAT, even if the person skilled in the art would have substituted known crystallisable lipid components as taught by Westesen in the emulsions of Jansen to prepare a drug delivery system, the solid particles would have not been monodisperse;

THAT, in Jansen (paragraph [0045]), emulsification equipment includes a wide variety of agitators, homogenisers, colloid mills, jet mixers and ultrasonic devices, with rotation speed usually above 2000 r.p.m.;

THAT, monodisperse lipid particles cannot be merely obtained by putting crystallisable lipid components as taught by Westesen in the emulsions of Jansen, which are mixed at a rotation speed above 2000 r.p.m.;

THAT, based on my specific research projects relating to lipid particles, I conclude that only application of shear such as in a Couette device having a gap of about 100 microns at a rotation speed comprised between 75 and 600 r.p.m and at an injection speed of 0.7 would have allowed to obtain monodisperse lipid particles ;

THAT, there is no suggestion in Jansen, nor in Westesen to use shear, much less a Couette device with rotation speed comprised between 75 and 600 r.p.m and with an injection speed of 0.7;

THAT, one of ordinary skill in the art would have understood, after considering the method taught in Jansen and crystallisable lipid components taught by Westesen, that the lipid particles resulting of this combination are fundamentally different structurally from the lipid particles of the pending claims, since they are not monodisperse; and that this structural difference involves a functional difference;

THAT, the lipid particles according to the present invention are monodisperse, such monodisperse particles have therefore an homogeneity of the granulometric distribution, which is very important in the context of oral administration, insofar as the size of the particles conditions (i) the rate of release of the active principle, (ii) the interactions with the gastrointestinal mucosa, (iii) the degradation by the digestive enzymes, the lipases, which is a surface phenomenon, and (iv) the passage of the particles through the intestinal epithelium is concerned.

I, the undersigned, declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and, further, that these statements were made with the knowledge that wilful false statements

Paris, 14 Octobre 2009.

Shiller